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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/583,923	05/14/2007	Manpreet S. Wadhwa	PC027698A	4848

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EXAMINER	
HAMUD, FOZIA M	

ART UNIT	PAPER NUMBER
1647	

MAIL DATE	DELIVERY MODE
04/29/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/583,923	WADHWA ET AL.	
	Examiner	Art Unit	
	FOZIA M. HAMUD	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 February 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

Response to Applicant's Amendment:

1a. Applicants' amendment filed on 20 February 2009 have been entered.

Status of Claims

1b. Claims 1-15 are pending and under consideration in the instant application.

Specification:

2. The amendment to the specification amending typographical errors is acknowledged. It is apparent from the data on table VII and figure 7 that methionine improved the chemical stability of the hGH liquid formulations in samples 26 and 27, in which PEG was present. No new matter has been introduced.

Response to Applicant's Argument:

3. The following rejections are withdrawn in light of Applicants' arguments:

I. The objection to claim 1 is withdrawn.

II. The amendment of claims 7, 11-15 has overcome the rejection of said claims made under 35 U.S.C. 112, first paragraph for not enabling the full scope of the claimed invention.

III. The amendment of claims 1, 2, 13 and 15 has overcome the rejection of said claims made under 35 U.S.C. 112, second paragraph.

III. The rejections of claims 1-6, 9-10 made under 35 U.S.C § 102(b) as being anticipated by WO97/29767, is withdrawn, because the McMAMARA et al reference does not disclose formulations of growth hormone that comprise methionine.

IV. The rejections of claims 1-6 are rejected under 35 U.S.C § 102(b) as being

anticipated by US20020077461, (BJORN et al published on 20 June 2002), is withdrawn, because BJORN et al reference does not disclose formulations of growth hormone that comprise methionine.

New Grounds of Rejections:

Claim Rejections - 35 USC § 103:

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over O'Connor et al (U.S. Patent 6,448,225, issued on 10 September 2002) in view of Patel, Suman, (US patent 5,358,708, issued on 25 October 1994).

The instant claims 1 is drawn to a formulation comprising a therapeutically effective amount of a human growth hormone, (recombinant) in an aqueous solution, a buffer that maintains the pH of the formulation at a pH of 5 to 7, a non-ionic surfactant, a

polymer stabilizer, methionine, and one or more optional excipients selected from the group consisting of a divalent cation present in a magnesium salt selected from the group consisting of magnesium hydroxide, magnesium chloride, magnesium sulfate, magnesium citrate, and magnesium edentate; a tonicity agent; and a preservative, wherein the formulation remains stable after at least one freezing and subsequent thawing event. Claims 2-12, recite specific concentrations and or excipients. Claim 13 encompasses that the formulation remains in solution after exposure to three or more freeze-thaw events, claims 14-15 further limit the invention regarding time that the formulation remains stable that total deamidaion is measured by anion exchange HPLC.

O'Connor et al teach a stable aqueous formulation of human growth hormone, (recombinant) comprising human growth hormone, citrate, phosphate, Tris, succinate, or histidine buffer, (2 mM to 50 mM), providing pH 5.5 to pH 7, nonionic surfactant, (polysorbate 20 or 80, 0.1% to 5%), polyethylene polymer, tonicity agent, (sorbitol) and preservative, (phenol or benzyl alcohol), (see column 3, lines 1-3 and column 3, line 30 to column 4, line 22). O'Connor et al teach that their formulation is stable upon storage for 6 to 18 months at 2 to 8^0 C and that deamidation was measured by anion exchange chromatography, (see column 5, line 51 to column 6, line 50).

However, O'Connor et al do not teach formulations of human growth hormone that also comprise methionine.

US patent 5,358,708, (Patel, Suman) teaches an aqueous formulations of an interferon, a granulocyte-macrophage colony-stimulating factor or an interleukin having

extended storage lifetimes by adding methionine to said formulations, (see column 3, line 59 to column 4, line 33, figures 1 and 2 and claims).

Therefore, it would have been obvious to the person of ordinary skill in the art at the time the invention was made, to modify the formulations of human growth hormone taught by O'Connor et al by adding methionine to said formulation by following the techniques taught by Patel, who teaches the benefit of using methionine to extend the storage lifetimes of formulations of recombinant proteins. One of ordinary skill would have achieved the predictable result of obtaining a stable liquid formulation with extended storage lifetime of any polypeptide with a great expectation of success by following the techniques taught by the O'Connor et al and Patel references. One of ordinary skill would have been able to manipulate concentrations of buffers and excipients to obtain optimum stability. The person of ordinary skill in the art would have been motivated to make an human growth hormone in a stable liquid formulation with extended storage lifetime, because growth hormone is used clinically to treat children's growth disorders and adult growth hormone deficiency and therefore, it is of great importance to obtain stable human growth hormone formulations with extended storage lifetime to improve efficacy and prevent undesirable byproducts such as aggregates during processing and storage. Accordingly, the invention, taken as a whole, is prima facie obvious over the cited prior art.

Conclusion:

6. No claim is allowed.

Advisory Information:

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fozia M. Hamud whose telephone number is (571) 272-0884. The examiner can normally be reached on Monday, Thursday-Friday, 6:00 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjuanth N. Rao can be reached on (571) 272-0939. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Fozia Hamud
Patent Examiner
Art Unit 1647
22 April 2009

/Bridget E Bunner/
Primary Examiner, Art Unit 1647